

Remarks

Status of the Claims

Claims 26-38 are pending in the present application. Applicants hereby cancel claims 28-33, and 36 without prejudice to Applicants' right to pursue their subject matter in this and related applications. Applicants have amended claims 26 and 27. Support for amended claims 26 and 27 is found in the specification at least, for example, from page 8, line 24 to page 9, line 7, and at page 10, lines 7-17 and 22-24. Accordingly, upon entry of these amendments, claims 26, 27, 34, 35, 37, and 38 will be pending and presented for consideration.

Interview

Applicants thank Examiners Jiang and Spector for the interview on March 15, 2004, discussing proposed amendments to the claims pending in this application. Applicants have amended the claims accordingly and submit that the claims are presently in condition for allowance.

The following comments address the claim rejections in the order that they were raised in the Office action.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 26-38 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. The Office action indicates that this rejection is based on Applicants' amendments to claims 26, 27, and 38, filed with the U.S. Patent and Trademark Office on November 5, 2003.

Applicants have canceled claims 28-33, and 36. Therefore, Applicants respectfully submit that the rejection of claims 28-33, and 36 under 35 U.S.C. § 112, first paragraph is moot.

Applicants respectfully traverse the rejection of claims 26, 27, 34, 35, 37, and 38 under 35 U.S.C. § 112, first paragraph. Applicants submit that the basis for the recitation of "at least a portion of an IgG3 chain constant region" is found in the specification at least, for example, at

page 10, lines 22-23, reciting, “Fc regions derived from gamma1 or gamma3 chains preferably are used in the Fc-X constructs of the invention.” Accordingly, Applicants request that the rejection of claims 26, 27, 34, 35, 37, and 38 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 26, 28-30, 34-36 and 38 are rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 5,723,125 to Chang *et al.* (“Chang”) in view of U.S. Patent No. 5,541,087 to Lo *et al.* (“Lo”). Claims 27, 31-33 and 37 are rejected under 35 U.S.C. § 103(a) over Chang and Lo, and in further view of U.S. Patent No. 5,116,964 to Capon *et al.* (“Capon”). Applicants respectfully traverse these rejections.

The pending claims, as amended, are drawn to methods of targeting an Fc fusion protein with interferon-alpha (IFN- α) to a liver tissue, while reducing an effect of an Fc effector function, by administering a fusion protein comprising, in an N- to C-terminal direction, an Ig Fc region and an IFN- α protein. Applicants’ invention is based in part on the discovery that the N- to C-terminal orientation of the Fc-IFN- α fusion protein impairs antibody-dependent cell-mediated cytotoxicity (ADCC) and complement fixation, but maintains preferential targeting to liver tissues (see, *e.g.*, page 10, lines 10-24 of the present application). The discovery of a fusion protein capable of targeting IFN- α to liver tissues while reducing an effect of an Fc effector function has not been taught or suggested prior to Applicants’ invention.

None of Chang, Lo, or Capon teaches or suggests methods of targeting an Fc fusion protein with IFN- α to a liver tissue while reducing an effect of an Fc effector function by administering an Fc-IFN- α fusion protein having a specific N- to C-terminal orientation. Indeed, none of the references teaches or suggests a method of targeting to a liver tissue an Fc-IFN- α fusion protein having impaired Fc effector function. The references do not teach or suggest that the N- to C-terminal orientation of an Fc-IFN- α fusion protein has any impact on effector function. Furthermore, none of the references provides any reasonable expectation of targeting an Fc-IFN- α fusion protein with reduced Fc effector function to a liver tissue by administering a

fusion protein having a specific N- to C-terminal orientation. Accordingly, even in combination, the references could not teach or suggest the claimed invention. Applicants therefore respectfully request that the rejection of the pending claims under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Conclusion

Claims 26, 27, and 34-38 are pending and believed to be in condition for allowance. Examiner Jiang is invited to telephone the undersigned attorney to discuss any remaining issues.

Respectfully submitted,



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